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Sequence Listing was accepted.

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Reviewer: markspencer

Timestamp: Wed Oct 31 14:45:30 EDT 2007

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Application No: 09955737 Version No: 3.0

**Input Set:**

**Output Set:**

**Started:** 2007-10-12 14:30:08.228  
**Finished:** 2007-10-12 14:30:08.767  
**Elapsed:** 0 hr(s) 0 min(s) 0 sec(s) 539 ms  
**Total Warnings:** 4  
**Total Errors:** 0  
**No. of SeqIDs Defined:** 15  
**Actual SeqID Count:** 15

Error code	Error Description
W 213	Artificial or Unknown found in <213> in SEQ ID (3)
W 213	Artificial or Unknown found in <213> in SEQ ID (4)
W 213	Artificial or Unknown found in <213> in SEQ ID (5)
W 213	Artificial or Unknown found in <213> in SEQ ID (6)

SEQUENCE LISTING

<110> Chopra , Rajiv  
Svenson, Kristine  
Annis, Bethany  
Akopian, Tatos N.  
Bard, Jonathan A.  
Stahl, Mark L.  
Somers, William Stuart

<120> CRYSTAL STRUCTURE OF BACE AND USES  
THEREOF

<130> 16163-015001

<140> 09955737  
<141> 2001-09-19

<150> US 60/234,576  
<151> 2000-09-22

<160> 15

<170> FastSEQ for Windows Version 4.0

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<211> 501  
<212> PRT  
<213> Homo sapiens

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
20 25 30  
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
35 40 45  
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
50 55 60  
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
65 70 75 80  
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
85 90 95  
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
100 105 110  
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
115 120 125  
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
130 135 140  
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
145 150 155 160  
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
165 170 175  
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp

180	185	190
Ser Leu Glu Pro Phe Phe Asp Ser	Leu Val Lys Gln Thr His Val Pro	
195	200	205
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln		
210	215	220
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile		
225	230	235
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg		
245	250	255
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln		
260	265	270
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val		
275	280	285
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala		
290	295	300
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp		
305	310	315
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr		
325	330	335
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val		
340	345	350
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg		
355	360	365
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala		
370	375	380
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu		
385	390	395
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala		
405	410	415
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu		
420	425	430
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro		
435	440	445
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala		
450	455	460
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp		
465	470	475
Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp		
485	490	495
Ile Ser Leu Leu Lys		
500		

<210> 2  
<211> 695  
<212> PRT  
<213> Homo sapiens

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20	25	30
Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln		
35	40	45
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp		
50	55	60
Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu		

65	70	75	80
Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn			
85	90	95	
Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val			
100	105	110	
Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu			
115	120	125	
Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys			
130	135	140	
Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu			
145	150	155	160
Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile			
165	170	175	
Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu			
180	185	190	
Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val			
195	200	205	
Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys			
210	215	220	
Val Val Glu Val Ala Glu Glu Glu Val Ala Glu Val Glu Glu Glu			
225	230	235	240
Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu			
245	250	255	
Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile			
260	265	270	
Ala Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg			
275	280	285	
Val Pro Thr Thr Ala Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu			
290	295	300	
Glu Thr Pro Gly Asp Glu Asn Glu His Ala His Phe Gln Lys Ala Lys			
305	310	315	320
Glu Arg Leu Glu Ala Lys His Arg Glu Arg Met Ser Gln Val Met Arg			
325	330	335	
Glu Trp Glu Glu Ala Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp			
340	345	350	
Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu			
355	360	365	
Gln Glu Ala Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala			
370	375	380	
Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn			
385	390	395	400
Tyr Ile Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe			
405	410	415	
Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His			
420	425	430	
Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala			
435	440	445	
Ala Gln Ile Arg Ser Gln Val Met Thr His Leu Arg Val Ile Tyr Glu			
450	455	460	
Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala			
465	470	475	480
Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn			
485	490	495	
Tyr Ser Asp Asp Val Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser			
500	505	510	
Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr			
515	520	525	

Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln  
530 535 540  
Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn  
545 550 555 560  
Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr  
565 570 575  
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser  
580 585 590  
Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val  
595 600 605  
His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys  
610 615 620  
Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val  
625 630 635 640  
Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile  
645 650 655  
His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg  
660 665 670  
His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys  
675 680 685  
Phe Phe Glu Gln Met Gln Asn  
690 695

<210> 3

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> APP inhibitor peptide

<220>

<221> VARIANT

<222> 5

<223> Xaa = Sta = Statine

<400> 3

Ser Glu Val Asn Xaa Val Ala Glu Phe

1 5

<210> 4

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 4

gctctagaac ccagcacggc atccggctg

29

<210> 5

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 5

ccaaggatgc ggccgcaata ggctatggtc atgagggttg ac

42

<210> 6

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetically generated peptide

<400> 6

Ser Glu Val Asn Leu Asp Ala Glu Phe Arg

1 5 10

<210> 7

<211> 390

<212> PRT

<213> Homo sapiens

<400> 7

Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln

1 5 10 15

Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn

20 25 30

Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro

35 40 45

His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr

50 55 60

Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp

65 70 75 80

Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn

85 90 95

Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe

100 105 110

Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala

115 120 125

Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu

130 135 140

Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly

145 150 155 160

Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly

165 170 175

Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu

180 185 190

Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val

195 200 205

Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr

210 215 220

Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu

225 230 235 240

Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser

245 250 255

Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val

260 265 270

Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
                  275                 280                 285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
                  290                 295                 300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
                  305                 310                 315                 320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
                  325                 330                 335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
                  340                 345                 350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
                  355                 360                 365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
                  370                 375                 380  
 Asp Cys Gly Tyr Asn Ile  
                  385                 390

<210> 8  
 <211> 390  
 <212> PRT  
 <213> Homo sapiens

<400> 8

Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly			
1                 5                 10                 15			
Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile			
20                 25                 30			
Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His			
35                 40                 45			
Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg			
50                 55                 60			
Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu			
65                 70                 75                 80			
Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val			
85                 90                 95			
Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe			
100                105               110			
Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu			
115                120               125			
Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val			
130                135               140			
Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala			
145                150               155               160			
Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser			
165                170               175			
Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp			
180                185               190			
Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg			
195                200               205			
Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn			
210                215               220			
Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro			
225                230               235               240			
Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser			
245                250               255			
Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys			
260                265               270			

Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu  
275 280 285  
Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu  
290 295 300  
Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp  
305 310 315 320  
Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met  
325 330 335  
Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg  
340 345 350  
Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe  
355 360 365  
Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp  
370 375 380  
Cys Gly Tyr Asn Ile Pro  
385 390

<210> 9  
<211> 150  
<212> PRT  
<213> Homo sapiens

<400> 9  
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Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
20 25 30  
Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
35 40 45  
His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
50 55 60  
Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
65 70 75 80  
Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
85 90 95  
Val Thr Val Arg Ala Asn